Remarks

Support for limitations in the claims in the present claim set

As noted in the previously filed Supplemental Amendment/Response of June 25, 2010, support for the limitations in the claims of the previous Amendment/Response of March 10, 2009 was cited on pp. 51-70 of that previous Amendment/Response. The limitations in the presently pending claims are, in general, not new and are the same or essentially the same, as limitations in the claim set of March 10, 2009. Therefore the Examiner is urged to consult the Remarks of previous Amendment/Response of March 10, 2009 on pp. 51-70 for detailed support in the present application 10/037,718, the PCT parent PCT/US99/04376, and Provisional priority application 60/076102 in terms of page and line number. In addition the Examiner is urged to consult similar detailed support for some claim limitations in the Remarks of the Brief Supplemental Response of July 3, 2009, pp. 2-5. Also similar detailed support for some claim limitations is present in the Remarks of the Preliminary Amendment of October 2, 2007, pp. 15-37.

The similar detailed support for some claim limitations cited above that is present in the Remarks of the Preliminary Amendment of October 2, 2007, pp. 15-37, refers, however, to numbered paragraphs in the published version of the present application, 10/037718. In addition, there are no citations in October 2, 2007 that refer to the PCT parent PCT/US99/04376 or the earliest provisional priority application 60/076102. For the Examiner's convenience, the applicants will now again cite support for claim limitations in the presently pending claims that was previously cited in the Preliminary Amendment of October 2, 2007. But this presently cited support will refer to page and line number in the present application 10/037718 as filed, in the PCT parent PCT/US99/04376 and in the earliest provisional priority application 60/076102.

Citing support in the present application 10/037718, the PCT parent PCT/US99/04376, and in the earliest provisional priority application 60/076102 will help show a chain of continuity in the support. The PCT parent, PCT/US99/04376 (filed 2/26/99), claims priority from Provisional priority application 60/076102 (filed 2/26/98). And each of the later filed parent U.S. National applications for the present application, 09/623068 filed 8/26/2000 and 09/947768 filed 9/5/2001, incorporate by reference the earlier filed PCT parent, PCT/US99/04376. The present application 10/037,718 also claims priority from Provisional priority application 60/076102.

In most or all cases the page and line numbers of the relevant sections of these applications will be cited. **For the sake of brevity the following abbreviations will be used:** "'718 app." for the present application 10/037,718, "PCT" for the PCT parent PCT/US99/04376, and "Prov. '102" for Provisional priority application 60/076102.

The cited support will be in accordance with the Written Description Requirement; MPEP 2163 states in part: *"To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116."*

Support for limitations in presently pending independent claims 91, 236, 300 and 303 that was previously cited, mostly in the Preliminary Amendment of October 2, 2007 and the previous Amend./Resp. of 3/10/2009.

For support for the claim limitation *"A composition for use in obtaining genotype data or sample allele frequency data, comprising: one or more copies*

of a set of oligonucleotides, the set of oligonucleotides being complementary to a group of two or more bi-allelic covering markers," see '718 app. p. 37 lines 3-22, PCT p. 35 line 27 to p. 36 line 17 and Prov. '102 p. 64 line 42-52. See also '718 app. p. 34 line 25 to p. 35 line 16, p. 35 line 35 to p. 36 line 27, PCT p. 33 line 20 to p. 34 line 11, p. 34 line 30 to p. 35 line 22, and Prov. '102 p. 60 lines 33-46, p. 52 line 46-53, p. 53 line 12 to p. 54 line 22.

For support for the limitation *"wherein the set of oligonucleotides is selected for the set's utility to determine genotype data or sample allele frequency data for each of the two or more covering markers"* See '718 app. p. 37 lines 8-22, PCT p. 36 lines 3-17, and Prov. '102 p. 64 lines 42-50. (It should be noted that genotype data for *"samples of individuals"* that are *"groups of individuals who have supplied phenotype data regarding the genetic characteristic and provided chromosomal DNA samples which have been pooled"* is sample allele frequency data; see for example Prov. '102 p. 36 lines 23-34.) (Support for this limitation was previously cited on p. 52 of the Amend./Resp. of 3/10/2009, but is repeated here now.)

For support for the limitation *"wherein the group of covering markers is chosen so that a CL-F region is N-covered to within [x, y] by the covering markers, wherein [x, y] is a two-dimensional distance….N is an integer greater than or equal to 1."* For support see for example, '718 app. p.14 lines 26-28, lines 33-37, PCT p. 13 lines 26-28, lines 33-37, and Prov. '102 p. 30 lines 45-47, lines 52-53, & p. 31 lines 2-4. (Support for this limitation was previously cited on pp. 52-53 of the Amend./Resp. of 3/10/2009, but is repeated here now.)

As explained on pp. 2 & 3 of the previous Brief Supplemental Response of July, 2, 2009 it is possible to claim the invention simply in terms of *"N covered to within [x, y]."* The support cited in the previous Brief Supplemental Response of July, 2, 2009 is repeated here now. The present application ('718 app.) contains numerous examples and Description text, in which the invention is described simply in terms of *"N covered to within [x, y]."* For example see example embodiments on p. 29 lines 16-17, p. 32 lines 20 & 31, p. 34 lines 15 & 21-22, p.

36 line 39 to p. 37 line 1 and p. 37 lines 20-21. Similarly the PCT parent also contains numerous examples in which the invention is described simply in terms of *"N covered to within [x, y]."* For example see example embodiments in PCT/US99/04376 on p. 28 lines 7-9, p. 31 lines 13, 24 & 30-31, p. 33 lines 10 & 16-17, p. 35 lines 34-35 and p. 36 lines 15-16. Similarly priority Provisional application (60/076102) also contains numerous examples in which the invention is described simply in terms of *"N covered to within [x, y]"* or *"N covered to within* δ*"* wherein δ is a two-dimensional distance that is or can be denoted as [x, y]. See for example Prov. '102 p. 34 lines 13-15, p. 40 lines 18-20, lines 44-45, p. 43 lines 40-41, p. 47 lines 37-39, p. 56 lines 39-41, lines 45-46, p. 59 lines 47-49, p. 60 lines 3-4, p. 64 lines 5-11, p. 65 lines 7-10, p. 67 lines 2-5 and lines 8-13.

For support for the limitation *"wherein x is less than or equal to 1 million base pairs and y is less than or equal to 0.2"* see for example '718 app. p.27 lines 20-23, lines 27-28, 32-33, p. 29 lines 16-17; PCT p. 26 lines 11-14, lines 18-20, p. 28 lines 7-8 and Prov. '102 p. 35 lines 14, 20-22, 44-46, p. 40 lines 18-20. (Support for this limitation was previously cited on p. 53 of the Amend./Resp. of 3/10/2009, but is repeated here now.)

For support for the claim limitation *"the covering markers and the CL-F region being for a species of creatures"* '718 app. p. 26 lines 26-27, p. 23 line 17; PCT p. 25 lines 18-19, p. 22 line 8; Prov. '102 in the Definition of a CL-F region *"species under study"* at p. 30 lines 33-34, Title of the Invention: Improved Techniques for Linkage Studies at p. 1 or in the Header at any page, *"in a species of creatures, comprising the steps of: choosing two or more bi-allelic covering markers so that a CL-F region is N covered"* at p. 34 line 11-13.

For support for the claim limitation *"the CL-F region being a collection of one or more points on a two-dimensional CL-F map that is similar to an x-y graph,"* see '718 app. p. 10 lines 26-27, lines 3-4; PCT p. 9 lines 26-27, lines 3-4; Prov. '102 p. 30 line 27, p. 29 lines 1-4.

For support for the claim limitation *"the CL-F map having the two orthogonal dimensions of chromosomal location (CL) and least common allele frequency*

(F)," It is well-known that an x-y graph has two orthogonal (i.e., at right angles) dimensions, x and y, see '718 app. p. 10 lines 3-8; PCT p. 9 lines 3-8; Prov. '102 p. 29 lines 1-4. P. 8 lines 8-11. See also Abstract of '718 app. & PCT.

For support for the limitation *"whereby each point in the region is within the distance [x, y] of each of N or more of the covering markers."* This whereby clause is not a true limitation, it follows from the other limitations in the claim and the definition of N-covering. See '718 app. p. 13 lines 34-36 & p. 14 lines 26-28, PCT p. 12 lines 34-36 & p. 13 lines 26-28 and Prov. '102 p. 30 lines 19-21, lines 45-47. (Support for this limitation was previously cited on p. 53 of the Amend./Resp. of 3/10/2009, but is repeated here now.)

For support for the other limitations in independent claims 91, 236, 300 and 303, see pp. 53-57 of the previous Amend./Resp. of 3/10/2009 as well as pp. 23-33 of the recent Amend./Resp. of June 25, 2010.

Support for some other claim limitations in pending claims 92, 236, 237, 300, 303.

For support for the limitation *"wherein the CL-F region is for the species of creatures and for a population, wherein the population is a population as in the field of population genetics"* see above for support for *"the CL-F region being for a species of creatures."* For *"for a population"* see for example '718 app. p. 20 lines 8-12, especially line 12, p. 23 line 22, p. 26 lines 26-27 & lines 37-39, PCT p. 19 lines 8-12, especially line 12, p. 22 line 13, p. 25 lines 18-19 & lines 29-31, and Prov. '102 p. 21 lines 45-56, p. 31 lines 20-28, and p. 34 lines 49-56. For *"wherein the population is a population as in the field of population genetics"* (the term population is used in a statistical sense and in the sense the term is used in population genetics), see for example, '718 app. p. 20 lines 23-25, PCT p. 19 lines 23-25; & '718 app. p. 44 lines 21-22, PCT p. 43 lines 21-25, (e.g., *"Finnish population"* and *"more genetically heterogeneous populations"*) and Prov. '102 p. 6 lines 41-42, p. 10 line 29 & 37, p. 21 lines 45-56, p. 31 lines 20-28, p. 36 lines 8-21, especially lines 13-14 (*"population genetics"*) and p. 75 lines 39-42.

For support for the limitation *"wherein each covering marker is an SNP"* see '718 app. p. 35 lines 10-13 & 23, PCT p.34 lines 5-8 & 18, Prov. '102 p. 27 line 51, p. 53 lines 42-43 (e.g., *"thousands of bi-allelic markers"*). For a person of ordinary skill in the art, SNPs would generally be immediately associated with the phrase *"thousands of bi-allelic markers,"* this is explained in more detail on p. 22 of the Amend./Resp. of March 10, 2009 by citing the 1997 Kruglylak reference, Kruglyak (The use of a genetic map of biallelic markers in linkage studies. Nature Genetics, September 1997, vol.17, pp. 21-24). This Kruglyak references discusses very large numbers of SNPs for use as bi-allelic markers in genetic studies.

Also references incorporated into the applications that support single base or single nucelotide polymorphisms. Specifically the (1) Chee reference recites *"single-base resolution"* in its Abstract and *"single-base polymorphism"* twice (in the mid left column and the bottom of middle column on p. 611). Similarly each of the three (2) Saiki, (3) Wu and (4) Nickerson references recite *"single base"* or *"single nucleotide"* variation in their introductions in the first (leftmost columns) of their first pages. More information on these references follows. See endnote references on p. 125 of Prov. '102 (and endnotes of '718 app. p.50, PCT p. 48):

(1) Accessing Genetic Information with High-Density DNA Arrays, Mark Chee, etal. Science, vol 274, Oct. 25, 1996 , pp. 610 – 614.

(2)Genetic analysis of amplified DNA with immobilized sequence- specific oligonucleotide probes, Saiki,et al. Proc Natl Acad Sci USA vol 86, pp.6230-6234.

(3)Allele-specific enzymatic amplification of β-globin genomic DNA for diagnosis of sickle cell anemia, Wu, et al., Proc Natl Acad Sci USA vol 86 pp 2757-2760.

(4)Automated DNA diagnostics using an Elisa-based oligonucleotide ligation assay, Nickerson, et al., Proc Natl Acad Sci USA vol 87, pp. 8923-8927.

These above four references (and several others) are incorporated by reference into all three applications: '718 app., PCT, & Prov. '102. In addition, reference (1) is listed as reference D1 in the Information Disclosure Statement of 5/19/2008 and a copy of the Chee reference was provided to the Examiner. And each of the

(2) Saiki, (3) Wu and (4) Nickerson references is listed in the IDS of June 2009 as one of references AH-AM on sheets 1 and 2.

Some additional remarks with respect to claims As stated in MPEP 2105 with regard to the Supreme Court decision Diamond v. Chakrabarty, (447 U.S. 303) *"A review of the Court statements above as well as the whole Chakrabarty opinion reveals: The Court enunciated a very broad interpretation of 'manufacture' and 'composition of matter' in 35 U.S.C. 101."* In the *Chakrabarty* opinion the Supreme Court decided that a new invented living micro-organism *"with markedly different characteristics from any found in nature" "constituted a 'manufacture' or a 'composition of matter' within the meaning of 35 U.S.C.S. § 101."* In the *Chakrabarty* opinion the Supreme Court stated: *"The U.S. Supreme Court reads the term 'manufacture' in 35 U.S.C.S. § 101 in accordance with its dictionary definition to mean the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery. Similarly, composition of matter is construed consistent with its common usage to include all compositions of two or more substances and all composite articles, whether they are the results of chemical union, or of mechanical mixture, or whether they are gases, fluids, powders or solids."*

In accordance with the *Chakrabarty* opinion, the claim term "composition" should be interpreted broadly.

Some examples of the use of the term "composition" in the art or similar arts

These examples below give issued U.S. Patent numbers followed by some example claims that use the term "composition," the same term that is used in the presently pending claims.

U.S. Patent 6,770,441

1. An array composition comprising: (a) a rigid support; (b) a molded layer with at least a first assay location comprising discrete sites, wherein each of said discrete sites is configured to hold a single microsphere, and wherein said molded layer is adhered to said rigid support; (c) an adhesive layer disposed between said rigid support and said molded layer; and (d) a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said sites.

U.S. Patent 6,942,968

1. A composition comprising: a) a substrate with a surface comprising discrete wells, wherein each of said wells is configured to hold a single microsphere; a) a reflective coating on the bottom of the wells; and c) a population of microspheres distributed in said wells.

2. A composition according to claim 1 wherein at least one of said microspheres comprises a bioactive agent.

10. An array composition comprising: a substrate with a surface comprising an array of wells, wherein each of said wells is configured to hold a single microsphere; a reflective coating on the bottom of the wells; and a population of microspheres disposed in said wells, wherein said microspheres are linked to a bioactive agent.

U.S. Patent 7,179,600

1. A composition comprising oligonucleotide probes having sequence ID NO. 1 to 14, respectively.

2. The composition according to claim 1, wherein each of the oligonucleotide probes is a probe for identifying a hepatitis C virus genotype.

3. The composition according to claim 1, wherein each of the oligonucleotide probes is immobilized on a matrix.

U.S. Patent 6,429,027

1. A composite array composition comprising: a) a substrate with a surface comprising a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and b) a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

2. A composition according to claim 1 wherein each of said assay locations comprises a substantially similar set of bioactive agents.

U.S. Patent 7,157,228

1. A composition for analyzing one or more nucleic acid sequences in a patient genomic sample and for identifying said patient providing the sample, said composition comprising a mixture of: a first set of oligonucleotides, wherein members of the first set have different sequences and said members are attached to beads which are associated with an optically distinguishable characteristic that identifies the sequences of the oligonucleotides attached thereto, the first set of oligonucleotides for identifying target nucleic acid sequences in the patient sample; a second set of oligonucleotides wherein

members of the second set have different sequences and said members are attached to beads which are associated with an optically distinguishable characteristic that identifies the sequences of the oligonucleotides attached thereto, the second set of oligonucleotides for identifying a number of marker sequences in the patient genomic sample, said marker sequences each including at least one polymorphic marker, the identification of said marker sequences providing for identification of said patient.

2. The composition of claim 1, wherein the mixture of beads is arranged in a planar array, and the position of individual beads in the array is not pre-determined.

3. The composition of claim 2, wherein the bead array comprises subarrays, with the oligonucleotides of the second set and oligonucleotides of the first set being located in different subarrays.

U.S. Patent 7,172,804

1. A composition comprising a microarray, wherein said microarray comprises a substrate surface coated with an organic film, wherein said organic film comprises agarose, wherein said organic film further comprises a plurality of capture-spots, and wherein each of said capture-spots comprises a population of capture particles covalently bound to said organic film, and wherein each of said capture particles comprises a solid phase particle and a plurality of capture reagents attached to the surface of said solid phase particle.

U.S. Patent 7,163,998

1. A particle composition comprising monodisperse polymer beads stabilized by vinylsulfonyl-functionalized polymers, wherein said vinylsulfonyl-functionalized polymers are grafted to the external surfaces of said beads and, wherein said

vinylsulfonyl-functionalized polymer is soluble in water, water-miscible solvents, or a mixture thereof, wherein said vinylsulfonyl-functionalized polymer comprises vinylsulfonyl or vinylsulfonyl precursor moieties grafted to the surface of said polymer bead, wherein said vinylsulfonyl-functionalized polymers are represented by Formula I: ##STR00005## wherein "G" represents a polymerized .alpha.,.beta.-ethylenically unsaturated addition polymerizeable monomer; "H" represents a vinylsulfone or vinylsulfone precursor unit monomer; and x and y both represent molar percentages ranging from 10 to 90 and 90 to 10.

U.S. Patent 6,156,501

1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising an array of a plurality of oligonucleotide analogue probes having different sequences, wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations and wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets with a similar hybridization stability across the array.

The applicants now rebut any presumption of Festo type surrender of equivalents (e.g., under the doctrine equivalents) in the scope of any amended claim in this claim set by virtue of any current claim amendment.

Conclusion

The applicants have filed a Brief Second Supplemental Response & Amendment following the recent submission of a Supplemental Amendment/Response on June 25, 2010.

Remarks to indicate support for claim limitations and ensure compliance with the Written Description Requirement have been made to help show a chain of continuity in the support from the present application 10/037718 through the parent PCT application, PCT/US99/04376 (filed 2/26/99) to the earliest Provisional priority application 60/076102 (filed 2/26/98). A single limitation in each of dependent claims 253-268 and 280-290 has been amended in the same way. And a grammatical type amendment has been made to claim 212. These amendments should not place any additional examination burden on the Examiner. The number of claims (76) and independent claims (4) is unchanged from the previously filed Amendment/Response of June 25, 2010 and the applicants respectfully submit that no fees are due.

For the reasons advanced above, applicants respectfully submit that the claims are now in condition for allowance and that action is earnestly solicited.

Respectfully submitted,

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